Dear Members of the U.S. Pharmacopeial Convention (USP) Compounding Expert Committee,

On behalf of the more than 13,800 dermatologists based in the United States, our organizations write to you concerning the second set of proposed revisions to the USP’s General Chapter <797> Pharmaceutical Compounding – Sterile Preparations. One in four Americans suffers from a skin disease. Dermatologists diagnose and treat more than 3,000 diseases, including skin cancer, psoriasis, immunologic diseases, and many genetic disorders. As dermatologists on the front lines fighting skin cancer and treating numerous skin diseases, we are advocating for our patients to have access to compounded medications, especially in-office preparations. We share the USP’s concerns about the safety of the medications prepared and administered to patients.

The current version of this chapter does not include an exemption for the urgent use of compounded sterile preparations (CSPs). USP representatives have shared they do not consider scheduled or non-emergency surgeries to be circumstances where the current immediate-use provision would apply. We appreciate that the USP proposed an exemption where the preparation of non-hazardous CSPs would be exempt from the standards in this chapter if administered within one hour of beginning the preparation (lines 24-28). This timeframe may be workable for some specialties, including the few occasions in dermatology where medications are diluted. Unfortunately, a longer timeframe or a preparation-specific exemption is needed for buffered lidocaine, which is the most commonly used local anesthetic depended on by dermatologists and other specialists for office-based procedures.

We also thank the USP for granting a meeting request by the American Academy of Dermatology Association (AADA), American College of Mohs Surgery (ACMS), American Medical Association (AMA), American Society for Dermatologic Surgery Association (ASDSA), and American Society for Mohs Surgery (ASMS) to discuss patient access to buffered lidocaine. The representatives of the Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC) will also be joining this meeting, which will take place on November 30. We are hopeful that this meeting will result in the accommodation in this chapter’s standards of a safe and effective practice by physicians and the clinical staff that they supervise to prepare and administer this in-office preparation to their own patients. We are asking for at least a twelve-hour exemption from compliance with the chapter’s standards so that buffered lidocaine can be prepared ahead of patient visits for that day to help ensure valuable time is not taken away from patient interaction.

**Patient Need for Buffered Lidocaine and Preparation in the Clinical Setting**
An in-office preparation especially important to the practice of dermatology is buffered lidocaine. The two medications that comprise buffered lidocaine, lidocaine with or without epinephrine and sodium bicarbonate, are both approved by the FDA. Sodium bicarbonate is added to lidocaine...
with or without epinephrine using aseptic technique to neutralize the pH of the preparation. This process is "buffering." The buffering of lidocaine significantly decreases the subjective pain of the injection and increases the onset of the local anesthesia for the patient. According to the American Academy of Dermatology’s “Guidelines for the use of local anesthesia in office-based dermatologic surgery”: “The addition of sodium bicarbonate to local anesthetic, particularly lidocaine with epinephrine, is recommended to decrease the pain of delivery by subcutaneous or intradermal infiltration.” The strength of this recommendation was given an “A” in this guideline meaning that the “[r]ecommendation [is] based on consistent and good quality patient-oriented evidence.” After this local anesthetic takes effect, dermatologists are then able to perform procedures such as biopsies, excisions, or Mohs micrographic surgery.

Dermatologists buffer lidocaine ahead of their patient visits for the day because multiple buffered lidocaine syringes are frequently administered throughout the day to perform procedures such as skin biopsies and skin cancer surgery. In the proposed revisions, a one-hour exemption is included but this exemption would not facilitate access to buffered lidocaine especially during skin cancer curative Mohs surgery which usually last much longer than an hour. The Mohs surgeon or his or her clinical staff would have to exit the sterile field, buffer the lidocaine, and then re-enter the sterile field. Having physicians, who are compounding a small volume of low-risk sterile preparations for their own patients as a part of patients' treatment plans that same day, comply with the chapter’s full requirements as if they were pharmacies or outsourcing facilities is unreasonable and burdensome. Without including an accommodation in the final version of this chapter, dermatologists will likely be forced to forgo buffering lidocaine resulting in significantly increased patient-reported pain when administering lidocaine with or without epinephrine. They may also be forced to refer their patients to surgeons who can have an anesthesiologist administer general anesthesia in a hospital setting.

Requiring dermatologists to obtain buffered lidocaine from pharmacies or outsourcing facilities is both cost-prohibitive and not logistically feasible especially for dermatologists who are in private practice. While remaining safe, we recognize that buffered and diluted lidocaine with epinephrine begins to lose its vasoconstrictive efficacy after seven days. While it is the best practice to use buffered lidocaine prior to this amount of time, requiring transit time between the pharmacy or outsourcing facility is unreasonable and can result in medical waste if the buffered lidocaine is not used prior to the beyond-use date (BUD) determined by the pharmacy or outsourcing facility. In addition, our organizations cannot in good faith encourage our member dermatologists to use outsourcing facilities that have deficiencies that FDA inspectors cited in a Form FDA-483 issued including those who have advertised dermatology products to our general memberships. Consequently, as they have done safely for years, dermatologists need to be

4 E.g., U.S. Food and Drug Administration Form FDA-483. Edge Pharmacy Services, LLC. Issued March 8, 2018. Available at:
able to continue to safely prepare buffered lidocaine and administer it to their own patients in the clinical setting without unreasonable burdens.

**Like in FDA Guidance, Physician Offices Should Not Be Treated the Same as Larger Compounding Facilities**

Released in January 2018, FDA’s 2018 Compounding Policy Priorities Plan provided, in part:

> These guidance documents will be followed by revised draft guidance describing examples of conditions that the FDA considers to be insanitary and in violation of the FD&C Act. This guidance will address concerns raised by some providers who compound small quantities of drugs in their offices for patient use, and as part of their routine clinical practice. This came up in the setting of certain dermatological procedures, for example. The FDA plans to better define the circumstances under which we believe drugs are being mixed and applied in a manner that creates negligible patient risk, and therefore wouldn’t be subject to the same compliance policy under the agency’s risk-based approach to implementing these requirements.\(^5\)

The FDA specifically mentioned in-office preparations used in dermatological procedures, highlighting that the medications prepared are in small quantities, in the office setting, and for the physicians’ patient use. The FDA acknowledged that the mixing and application of these in-office preparations are of negligible patient risk and physicians should not be subject to the same standards as larger compounding facilities. As a result, it proposed in its revised draft guidance on Insanitary Conditions for Compounding Facilities that physician offices would not be included in its definition of compounding facilities, and that it generally did not intend to take enforcement action against physicians who were compounding in the office setting and administering or dispensing to his or her own patients.\(^6\) We ask that the USP consider the same factors as FDA highlighted – namely: small quantities, office setting, own patient use, routine clinical practice, negligible patient risk – when deciding how to facilitate patient access to CSPs prepared in the clinical setting, especially buffered lidocaine.

**Peer-Reviewed Journal Articles Support the Safety of Buffered Lidocaine**

Dermatologists share USP’s concern about the safety of compounded sterile preparations and have performed and rely upon studies published in peer-reviewed journal articles supporting the safety of buffered lidocaine specifically. Pate et al. found that syringes filled with lidocaine; lidocaine and epinephrine; lidocaine with sodium bicarbonate; and lidocaine, epinephrine, and sodium bicarbonate and stored for up to four weeks, when prepared using aseptic technique and when stored in controlled room and controlled cold temperatures, are not prone to bacterial growth.

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or fungal contamination. Zero of the 160 samples showed growth where streaked. This study had a larger sample size than a 1999 study, where 36 syringes of buffered lidocaine with epinephrine and sodium bicarbonate stored in room temperature were also not prone to bacterial or fungal contamination.

Lidocaine and other local anesthetics used in dermatology have antimicrobial properties. The sodium bicarbonate that the lidocaine with epinephrine is mixed with has been found to enhance the bactericidal effect of lidocaine. Dermatologists, pharmacists, and other researchers have also performed other studies that support stability as well as effectiveness of buffered lidocaine.

Our organizations appreciate the USP Compounding Expert Committee considering our comments as it finalizes revisions to the General Chapter <797> Pharmaceutical Compounding – Sterile Preparations. We hope that you will finalize at least a 12-hour exemption for buffered lidocaine because it does not present a risk to patient safety when prepared in the clinical setting but would adversely impact patients if not accessible. If you have any questions or would like additional information or to discuss, please contact Natasha Pattanshetti, JD, MPH, manager, regulatory policy at npattanshetti@aad.org or (202) 712-2618.

Sincerely,

American Academy of Dermatology Association
American College of Mohs Surgery
American Society for Dermatologic Surgery Association
American Society for Mohs Surgery
Alabama Dermatology Society
California Society of Dermatology & Dermatologic Surgery
Georgia Society of Dermatology & Dermatologic Surgery

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Indiana Academy of Dermatology
Illinois Dermatological Society
Iowa Dermatological Society
Maine Dermatologic Society
Maryland Dermatologic Society
Michigan Dermatological Society
Mississippi Dermatology Association
Missouri Dermatological Society Association
Nevada Society for Dermatology and Dermatologic Surgery
North Carolina Dermatology Association
Ohio Dermatological Association
Pennsylvania Academy of Dermatology and Dermatologic Surgery
Texas Dermatological Society
Utah Dermatology Society
Utah Medical Association
Washington DC Dermatological Society
Washington State Dermatology Association
Wisconsin Dermatological Society

cc: Suzanne Olbricht, MD, FAAD, President, AADA
Elaine Weiss, JD, CEO & Executive Director, AADA
Barbara Greenan, Senior Director, Advocacy and Policy
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